REMARKS

Claims 1 and 4-27 are pending. Claims 12-22 have been withdrawn from further consideration. Claims 1-3, 11, 23, 24, and 27 are canceled herein, without prejudice towards future prosecution of these claims. Claims 4-9, and 25 are amended herein. New claim 28 has been added. Applicants respectfully request entry of the amendments as they will place the claims in condition for allowance and/or place the claims in better form for appeal, if necessary.

Claims 4-8 and 25 have been amended to depend from allowed claim 26. Claim 4 has also been amended to recite, "a modified antibody . . . wherein said modification is selected from amino acid substitution and chemical modification." Support for recitation of "amino acid substitution" can be found on pages 57-62, 64-66, and 67-69 of the specification, which describe methods for making antibodies with amino acid substitutions and assays for testing the antigen binding and neutralization functions of these modified antibodies. Support for recitation of "chemical modification" can be found on page 14 of the specification, which recites, "[t]he modified antibodies can be prepared by chemical modifications of the antibodies. The chemical modification techniques suitable for this purpose have already been established in the art." Thus, no new matter has been added.

Claim 5 has also been amended to recite, "wherein the antibody is a humanized, human, or chimeric antibody." Support for this amendment can be found in the specification, for example, at the paragraph bridging pages 3 and 4.

Claim 9 has been amended to recite, "at least one anti-PTHrP antibody, or binding fragment thereof" and "wherein the antibody, or binding fragment thereof, binds specifically to SEQ ID NO:75." Support for this amendment can be found in the specification, for example, at page 5, lines 19-21, and at SEQ ID NO:75 in the Sequence Listing. Thus, no new matter has been added.

New claim 28 has been added. Support for recitation of "polyethylene glycol (PEG) conjugation" can be found in the paragraph bridging pages 13-14 of the specification, which recites, "[a]s a modified form of the above-mentioned antibodies, for example, anti-PTHrP antibody conjugated to any molecule (e.g., polyethylene glycol; PEG) may also be used. Such modified antibodies can be prepared by chemical modifications of the antibodies. The chemical modification techniques suitable for this purpose have already been established in the art." Support for recitation of "thyroglobulin conjugation" can be found page 23 of the specification, which recites, "PTHrP (1-34) (Peninsula) was conjugated with a carrier protein thyroglobulin using carbodiimide (Dojinn)." Thus, no new matter has been added.

Applicants acknowledge with appreciation that claim 26 is allowed and that claim 6 is allowable, if amended to no longer depend from a rejected claim. Accordingly, claim 6 has been amended to depend from allowed claim 26, thus placing claim 6 in allowable form. Applicants note that several rejections were not maintained in the present Office Action and are therefore, with appreciation, deemed withdrawn:

1. rejections of claim 6 under 35 U.S.C. § 112 ¶¶ 1 and 2 for enablement and written description;
2. rejection of claims 1, 4-8, and 23-27 under § 112 ¶ 2 for indefiniteness;
3. rejection of claims 1, 5-11, and 26-27 under 35 U.S.C. § 102e in view of U.S. Pat. No. 6,903,194;
4. rejection of claims 1, 4, and 25 under 35 U.S.C. § 103a in view of U.S. 6,903,194 combined with Harlow et al. or U.S. Pat. No. 4,946,778;
5. rejection of claims 23-24 under 35 U.S.C. § 103a in view of U.S. Pat. No. 6,903,194 combined with Harlow et al. and Kitamura et al;
6. rejection of claims 1, 4, 5, 7-11, and 23-25 under 35 U.S.C. § 103a in view of Yamamoto et al. combined with Sato et al., Harlow et al., and Hotta et al.
7. rejection of claim 5 under 35 U.S.C. § 103a in view of Yamomoto combined with Sato et al., Harlow et al., Hotta et al., and U.S. Pat. No. 6,180,370B;
8. rejection of claims 23-24 under 35 U.S.C. § 103a in view of Yamomoto combined with Sato et al., Harlow et al., Hotta et al., and Kitamura et al.; and

9. rejection of claim 25 under 35 U.S.C. § 103a in view of Yamomoto combined with Sato et al., Harlow et al., Hotta et al., and U.S. Pat. No. 4,946,778.

Formal Matters

Applicants note that the Office had not previously rejected claim 27 under 37 U.S.C. § 112 ¶ 1. Furthermore, the current rejection of claim 27 under 37 U.S.C. § 112 ¶ 1 was not necessitated by the Applicant's response filed on February 23, 2006. Thus, the rejection of claim 27 constitutes a new rejection and, therefore, the Action dated May 18, 2006, was improperly marked as "final." Accordingly, Applicants respectfully request that the Office withdraw the finality of the Action.

In Item 4 of the Office Action, the Office objects to claim 11 for allegedly reciting non-elected embodiments. Claim 11 has been canceled without prejudice towards future prosecution of the subject matter of this claim. Thus, the Office's objection to this claim is moot.

Rejections Under 35 U.S.C. § 112

Claims 1, 4, 5, 7-11, and 23-25 are rejected under 35 U.S.C. § 112 ¶¶ 1 and 2, and claim 27 is rejected under 35 U.S.C. § 112 ¶ 1. In Item 6 of the Office Action, the Office argues that the specification does not enable "any anti-PTHrP

antibody, any modified form of any antibody binding fragment, [or] any humanized, or chimeric antibody." (Office Action page 2, emphasis added.) Likewise, in Item 7 of the Office Action, the Office alleges that the specification does not provide written description for "any antibody such as any monoclonal, humanized, chimeric, antibody fragment and any 'modified form' of said fragment that binds to *all* 'PTHrP' and *any* part of PTHrP other than N-terminal 1-34." (Office Action page 7.) Applicants respectfully traverse.

Claims 1, 11, 23, 24, and 27 are cancelled solely to facilitate prosecution and without surrendering the subject matter of these claims, thus rendering the rejections of these claims moot. As currently amended, claims 4, 5, 7, 8, and 25 depend from allowed claim 26, thus incorporating all of the allowed limitations of claim 26. Furthermore, claim 9 has been amended to incorporate the allowable limitations from claim 26 of "at least one anti-PTHrP antibody, or binding fragment thereof" and "wherein the antibody, or binding fragment thereof, binds specifically to SEQ ID NO:75." By the Office's own admission, currently amended claims 5, 7-10, and 25 are enabled and meet the written description requirement:

- with regard to claims 5, 9, and 25, the Office states that the specification describes and enables a method of ameliorating low vasopressin levels comprising administering to a patient a humanized, human, or chimeric antibody, or antigen binding fragment thereof, that binds specifically to the N-terminal 1-34

amino acids of human PTHrP consisting of SEQ ID NO: 75. (Office Action at pages 2 and 7.);

- with regard to claim 7, the Office states that the specification discloses and enables a monoclonal antibody that binds to human PTHrP (1-34) consisting of SEQ ID NO: 75. (Office Action, page 4.); and
- with regard to claims 8 and 10, the Office states that the specification describes and enables a method of ameliorating low vasopressin levels resulting from cancer. (Office Action at page 6 and the sentence bridging pages 7-8.).

Thus, as currently amended, claims 5, 7-10, and 25 satisfy the enablement and written description requirements of 35 U.S.C. § 112 ¶¶ 1 and 2. Accordingly, Applicants respectfully request that the rejections of these claims be withdrawn.

With regard to the 35 U.S.C. § 112 ¶¶ 1 and 2 rejections of claim 4, the Office argues that the phrase "modified form" encompasses embodiments which are not supported in the specification. Specifically, the Office argues that "enablement is not commensurate in scope with the method of maintaining or increasing low vasopressin level in which any one or more modified antibody binding fragment to any PTHrP is administered to a patient." (Office Action page 7.) The Office also argues that there "is lack of written description about amino

acids within the binding region of the antibody fragment (CDRs) to be modified." (Office Action page 9.) Applicants respectfully traverse.

As currently amended, claim 4 recites, "a modified antibody . . . wherein said modification is selected from amino acid substitution and chemical modification." In one embodiment of amended claim 4, the antibody is modified by "amino acid substitution." Reference Example 4 (Specification pages 47-67) teaches methods for making antibodies modified by amino acid substitution. Nineteen modified antibodies are disclosed, encompassing 50 amino acid substitutions. Reference Example 4 also teaches the determination of antigen-binding ability for the modified antibodies and Reference Example 5 (Specification pages 67-69) teaches the determination of neutralizing activity for the modified antibodies. Thus, contrary to the Office's arguments, the specification provides ample guidance "as to which amino acids within the binding region of the antibody fragment (CDRs) to be modified." (Office Action pages 7 and 9.) For example, the specification states, "it was found that, among the humanized antibodies having the same levels of antigen-binding activity as that of the chimeric antibody, those antibodies having L-chain versions . . . (in which the 91-position tyrosine was replaced by isoleucine) exhibited the similar neutralizing activity to that of the chimeric antibody." (Specification page 68.)

In another embodiment of amended claim 4, the antibody is modified by "chemical modification." Reference Example 1 (Specification pages 23-24) teaches methods for producing chemically conjugated modified antibodies.

Specifically, this example teaches the preparation of an anti-PTHrP (1-34) antibody conjugated with a thyroglobulin carrier protein using carbodiimide (Dojinn). The specification also teaches that "[t]he modified antibodies can be prepared by chemical modifications of the antibodies" and that "[t]he chemical modification techniques suitable for this purpose have already been established in the art." (Specification page 14.)

Furthermore, Applicants submit that those skilled in the art would recognize that other chemical modifications are inherently embodied by claim 4, and as such, need not be specifically taught in the specification to satisfy the enablement and written description requirements of 35 U.S.C. § 112 ¶¶ 1 and 2. (*See generally*, MPEP §§ 2163 and 2164.) However, to comply with the Office's suggestion on page 9 of the Office Action, Applicants have also added new claim 28 to recite specific embodiments of chemically modified antibodies.

In view of the foregoing discussion, Applicants submit that, as currently amended, claim 4 satisfies the enablement and written description requirements of 35 U.S.C. § 112 ¶¶ 1 and 2. Accordingly, Applicants respectfully request that the rejections of this claim be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request that this Amendment be entered by the Office, thereby placing claims 5-10, 25, 26, and 28 in condition for allowance. Applicants submit that the

proposed amendments of claims 5-9 and 25 and the addition of new claim 28 do not raise new issues or necessitate the undertaking of any additional search of the art by the Office, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner. Finally, Applicants submit that the entry of the amendment would place the application in better form for appeal, should the Office dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, satisfies the enablement and written description requirements of 35 U.S.C. § 112. Applicants therefore request the entry of this Amendment, the Office's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: November 16, 2006

By: Rebecca M. McNeill
Rebecca M. McNeill
Reg. No. 43,796